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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,809	04/26/2002	Ronit Eisenberg	026549-000100US	1519

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EXAMINER	
CROWDER, CHUN	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/009,809	EISENBERG ET AL.	
	Examiner	Art Unit	
	Chun Crowder	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-70 and 72-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63-70 and 72-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 28, 2007, has been entered.

2. Applicant's amendment to the claims, filed on June 28, 2007, is acknowledged.

Claims 1-62, 71, and 80 have been canceled.

Claims 63-70 and 72-79 are pending and currently under consideration as they read on the originally elected invention of species of peptide without secondary complex, SEQ ID NO:1 as the first agent with first segment being SEQ ID NO:3, and condition of asthma.

3. Applicant is once again advised that should claim 79 be found allowable, claim 79 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 79 is once again objected to under 37 CFR 1.75 as being exact duplicate of claim 77.

Applicant is required to cancel the duplicate claim 79.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 63, 66-70, and 72-79 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Holgate et al. (British Medical Bulletin. 1992. 48;1:40-50) in view of Adridor et al. (Science 1993. 262:1569-1572) and Lin et al. (US Patent 5,807,746) for the same reasons set forth in the Office Actions mailed on August 2, 2006 and March 1, 2007.

The Office Action mailed on August 2006 states:

"Holgate et al. teach that mast cells degranulation has long been associated with asthma and pharmacological agents that can suppress the release of mast cell mediators have been shown to be clinical effective in treating IgE-dependent asthma and other forms of asthma where IgE dependent mechanisms have not been invoked (see entire document, particularly pages 40-47).

The reference teachings differ from the claimed invention by not describing a complex having peptide having amino acid sequence of SEQ ID NO:3 linked to peptide of SEQ ID NO:1.

However, the role of the peptide KNNLKECGLY (SEQ ID NO:1) in inhibiting mast cell degranulation was well know at the time the invention was made. For example, Adridor et al. teach that synthetic peptide KNNLKECGLY corresponding to the C-terminal end of protein $G\alpha_{i3}$ inhibits permeabilzed mast cell degranulation induced by synthetic compound 48/80 (see entire document, particularly page 1570 and Figure 2). Adridor et al. further teach that peptide KNNLKECGLY was ineffective when added to intact cells indicating that the target for the peptide was intracellular (e.g. see pages 1570-1571).

The methods for importing biological active molecules into cells were also well known in the art at the time the invention was made. Lin et al. teach a complex comprising importation competent signal peptides, such as membrane-permeable signal peptide of AAVALLPAVLLALLAP derived from Kaposi fibroblast growth factor, linked to a biological active molecule such as a peptide can be administered ex vivo or in vivo to treat diseases (see entire document, particularly Description of the Preferred Embodiments on columns 3-11).

Lin et al. further teach that importation competent signal peptides can be linked to the biological active molecule by peptide bond (e.g. see column 7). Furthermore, Lin et al. teach that the importing methods use mechanisms naturally occurring in cells thus avoiding damaging the target cells and can be used to import molecules into large numbers of cells including organs providing treatments of diseases (e.g. see columns 1 and 2).

It would thus have been obvious to the ordinary artisan at the time the invention was made to develop methods of inhibiting mast cell degranulation using synthetic peptide KNNLKECGLY corresponding to the C-terminal end of protein $G\alpha_{i3}$ linked to a importation competent signal peptide AAVALLPAVLLALLAP derived from Kaposi fibroblast growth factor for intracellular delivery. The ordinary artisan would have been motivated to do so because mast cell degranulation was associated with asthma and pharmacological agents that can suppress the release of mast cell mediators have been shown to be clinical effective, and synthetic peptide KNNLKECGLY targeting intracellularly was a well known agent in inhibiting mast cell degranulation and importation competent signal peptide AAVALLPAVLLALLAP could be linked to peptides to facilitate delivery peptides into cell using naturally occurring mechanisms.

Given the teachings of Holgate et al regarding the role of mast cell degranulation in asthma, and the teachings of Adridor et al. and Lin et al. providing the method of inhibiting mast cell degranulation by synthetic peptide KNNLKECGLY and methods of delivering biological molecule into cell using of importation competent signal peptide AAVALLPAVLLALLAP, the ordinary artisan at the time the invention was made would have had a reasonable expectation of success in producing the claimed methods."

Applicant's arguments including the Table shown on page 7 of the Remark filed on June 28, 2007, in conjunction with the declarations, under 37 C.F.R. 1.132, by Sagi-Eisenberg and Razin, have been fully considered but have not been found persuasive.

Applicant argues that the data disclosed in the instant specification and the experimentation taught by Jones et al. (Biochimica et Biophysica Acta 2005 1745:207-214, on PTO-892 mailed on August 2, 2006), as summarized in the Table on page 7 of the Remark filed on June 28, 2007, demonstrated unexpected surprising and advantageous results of the instant claimed invention. Applicant further asserts that the functionality of the CPP-fused cargo peptides Gαt or $G\alpha i_3$ to inhibit mast cell secretion is unpredictable. Furthermore, applicant asserts that of four CPP's tested, only the KFGF peptide is suitable for delivery of the mast cell inhibiting proteins and applicant assets that this was a surprise and obvious advantage over the prior art.

This is not found persuasive for following reasons:

Contrary to applicant's assertion that instant claimed invention presents unexpected, surprising results, it is noted that the claims are drawn to specific amino acid sequences, it was known in the art at the time the invention was made that the claimed the KFGF peptide AAVALLPAVLLALLAP (instant claimed SEQ ID NO:3) is capable of not only importing signal sequence-containing peptides but also maintaining the functions of the transported cargo peptides (see Lin et al, see columns 14-17 in particular); it was also known in the art that the peptide KNNLKECGLY (SEQ ID NO:1) can inhibit mast cell degranulation when penetrated into mast cell (see Adridor et al, particularly page 1570 and Figure 2). It would have been obvious to one having ordinary skill in the art to combine the two peptides to achieve the predictable results of inhibiting mast cell degranulation.

Further, in contrast to applicant's reliance on the Table on page 7 of the Remark and the Sagi-Eisenberg and Razin declarations to shown unexpected results, it is noted the data presented on said Table regarding CPPs that are not being claimed is appear to be irrelevant in the instant application because the instant claims are drawn to methods of inhibiting mast cell degranulation using the KFGF peptide AAVALLPAVLLALLAP (instant claimed SEQ ID NO:3) and the mast cell inhibitory cargo peptide KNNLKECGLY (instant SEQ ID NO:1).

Therefore, the human integrin β3 (Hu Int) and Kaposi fibroblast growth factor (KFGF), a Drosophila transcription factor (Dros), and transportan 10 (TP-10) (Jones et al. Biochimica et Biophysica Acta 2005. 1745:207-214, see page 207 in particular. Reference on PTO-1449) appear to be not relevant because they are not being claimed. In fact, applicant's own data appears to further demonstrate what has been taught by Lin et al. in that the KFGF peptide AAVALLPAVLLALLAP (instant claimed SEQ ID NO:3) is predictable in importing signal sequence-containing peptides and maintaining the functions of the transported cargo peptides. Thus, the KFGF peptide AAVALLPAVLLALLAP (instant claimed SEQ ID NO:3) has been consistently demonstrated in prior art as well as applicant's own data to be able to import biological peptides into the cells and maintain the functions of the transported peptides.

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 550 U.S. , 2007 U.S. LEXIS 4745, 2007 WL 1237837, at *12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

In this case, all the claimed elements including SEQ ID NOs: 1 and 3 were known in the prior art and one skilled in the art would have combined the elements as claimed by known methods with no change in their respective functions of importing peptides and inhibiting mast cell degranulation and the combination would have yielded predictable results to one of ordinary skill in the art at the time of invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments have not been found persuasive.

6. Claims 64 and 65 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Holgate et al. (British Medical Bulletin. 1992. 48;1:40-50) in view of Adridor et al. (Science 1993. 262:1569-1572) and Lin et al. (US Patent 5,807,746) as applied to claim 63 above, further in view of Avruch et al. (US Patent 6,103,692) and Jackson et al. (J. Am. Chem. Soc. 1994. 116:3220-3230) for the same reasons set forth in the Office Action mailed 08/02/2006 and March 1, 2007.

Applicant's arguments and the examiner's rebuttal are essentially the same as above in Section 5.

7. Claims 63-70 and 72-79 are provisionally rejected on the ground of **nonstatutory obviousness-type double patenting** as being unpatentable over claims 1-44 of copending USSN 10/465,826, and claims 1-15 of the copending USSN 11/214,588 for the same reasons set forth in the Office Action mailed 08/02/2006 and March 1, 2007.

Applicant argues that the rejection on the ground of provisional double patenting must be withdrawn when it is the sole remaining basis for rejection.

Given that the rejections under 35 U.S.C. 103(a) have been maintained for reasons stated above in Sections 7 and 8 and a terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) has not been filed; the rejection on the basis of double patenting will be maintained until such a time that allowable subject matter is determined or a terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) is timely filed.

8. *No claim is allowed.*

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chun Crowder whose telephone number is (571) 272-8142. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chun Crowder, Ph.D.
Patent Examiner
August 31, 2007

Maher M. Haddad
MAHER M. HADDAD
PRIMARY EXAMINER